SEQ ID NO:39. Claim 40 was amended to remove the pharmaceutically acceptable carrier. No new matter has been added.

Rejections Under 35 U.S.C. 112, First Paragraph

The Examiner rejected claims 1, 8, 9, 18, 19, 51-56 and 60 under 35 U.S.C. 112, first paragraph for an inadequate written description. Applicants respectfully traverse the rejection.

The Examiner's rejection stems from an alleged lack of objective evidence that the reading frame of the disclosed sequences are the correct reading frames, and that the sequences of the nucleic acid and protein encoded thereby are full length. Office Action at page 5.

Applicants maintain that they have, in fact, disclosed sufficient information to convey to one of ordinary skill in the art that they were in possession of the claimed invention, a nucleic acid molecule that encodes a sarcoma associated antigen. For example, in Example 3, Applicants stated:

> "The complete sdph3.10 cDNA clone was sequenced and found to be 2021 nucleotides long (SEQ ID NO:38) inclusive of the poly A tail, or about 2000 nucleotides long without the poly A tail. An open reading frame runs through the cDNA, with the first ATG at nucleotide 119 and a stop codon at nucleotide 1832. It encodes a putative protein of 571 amino-acids (SEQ ID NO:39).

In Example 5, Applicants similarly stated:

> The complete sdp3.5 cDNA clone was sequenced and found to be 2473 bp long (SEQ ID NO:43). An open reading frame runs through the cDNA, with the first ATG at nucleotide 79 and a stop codon at nucleotide 1660. It encodes a putative protein of 527 amino acids (SEQ ID NO:44), rich in leucine heptad repeats.

Applicants therefore described the characterized cDNA clones as complete and full length, and provided the person of skill in the art with the dimensions of the open reading frame, including the full length translation. Thus Applicants clearly have disclosed sufficient information about the reading frame, full-length sequence and encoded protein to convey to one of ordinary skill in the art that they were in possession of the claimed nucleic acid molecules.

The Examiner suggests on page 5 of the Office Action that Applicants have not sufficiently described the invention because "the predicted amino acid sequence may or may not be reflective or [sic, of] a true, in frame and expressed protein." To provide such information, and the other information suggested by the Examiner as necessary to definitively identify the

encoded polypeptides (e.g., molecular weight, shape, membrane association, etc.), Applicants would have had to engage in research which is not required to know that Applicants were in possession of the claimed invention. Such additional information about the expressed protein is not required for one of ordinary skill in the art to provide enough information to meet the requirements of 35 U.S.C. 112, first paragraph.

The legal standard for an adequate written description, that one of ordinary skill in the art would know that Applicants were in possession of the claimed invention, surely is met by the disclosure of the instant application. Applicants have provided nucleotide sequences and have shown that they contain open reading frames that begin with methionines and end with termination codons. Applicants have predicted the amino acid sequences encoded by the open reading frames of the sdph3.10 and sdp3.5 sequences, as is standard procedure in the art. Applicants have demonstrated that the sdph3.10 and sdp3.5 nucleotide sequences are expressed in a variety of tumors. One of ordinary skill in the art would conclude, reasonably, that Applicants have demonstrated all that is needed to show that they were in possession of the claimed invention.

The Examiner also rejected claim 40 under 35 U.S.C. 112, first paragraph as not enabled. Applicants have amended claim 40, and respectfully request reconsideration.

The Examiner has made several comments that Applicants wish to address. First, the Examiner stated that "[t]he quantity of experimentation necessary to identify such a composition would be a herculean task to accomplish, especially since as noted in the previous office action that the nucleic acid is merely associated with tumors and the specification is silent on what specific tumors could such a composition would be effective against." Sic, Office Action at page 6. If Applicants understand this statement, the Examiner meant to say that the quantity of experimentation would be undue, because Applicants' specification does not contain a description of tumor-associated expression of the sdph3.10 and sdp3.5 nucleic acid sequences such that one of ordinary skill in the art would know which tumors to test the composition in.

Applicants respectfully request that the Examiner reconsider the working examples provided in the specification. In particular, Examples 2 and 4 (see Tables III and V) show that the nucleic acid sequences are indeed expressed in specific tumor tissue samples. Accordingly, the Examiner's statement that the specification is "silent" on targets of an antisense composition

is incorrect. Moreover, Applicants have provided one of ordinary skill in the art with a set of tumors to test antisense compositions against, thus reducing the "herculean" amount of experimentation to an amount that can only be characterized as routine. In the relevant art, testing antisense compositions against specific types of tumors is within the routine effort of one of ordinary skill in the art. It is not Applicants' burden to provide a description of the steps used to test the antisense compositions for meeting FDA approval.

Rejections Under 35 U.S.C. 112, Second Paragraph

The Examiner rejected claims 1, 18, 19, [40,] 41, 43, 51-58 and 60 under 35 U.S.C. 112, second paragraph as indefinite. Applicants have amended some of the claims to overcome the rejections, and traverse other rejections, as described below.

The Examiner rejected claims 1 and 40 for the recitation of hybridization under stringent conditions. Applicants are aware that limitations cannot be read into claims from the specification. That consideration is not relevant with respect to the definiteness of the claims. instead, it appears that the Examiner is requiring the addition of a definition of a claim term from the specification, and on that basis, Applicants respectfully traverse the rejection.

Indefiniteness of the claims in relation to the specification was discussed in relation to biological properties: "...under the law pertaining to indefiniteness -- 'if the claims, read in light of the specification, reasonably apprise those skilled in the art both of the utilization and scope of the invention, and if the language is as precise as the subject matter permits, the courts can demand no more,' -- the claims are clearly definite. *Hybritech v. Monoclonal Antibodies* 802 F.2d 1367, 1385 (Fed. Cir. 1986). Accordingly, Applicants request that the rejection relating to the claims term "hybridize" be withdrawn.

Applicants have amended claim 1 to more clearly state that the claimed nucleic acids are related by degeneracy of the genetic code to SEQ ID NO:38 or SEQ ID NO:43, and that the hybridization is to a nucleotide sequence selected from the recited group of sequences.

The Examiner rejected claims 1 and 60 as indefinite for the use of the term "sarcoma associated gene product". Although Applicants believe that the term was sufficiently clear and definite to one of ordinary skill in the art, these two claims have been amended to recite an

alternative term "tumor associated gene product". Claims 40, 41, 43 and 50 also were rejected for use of the terms tumor associated nucleic acid/ and polypeptide.

A tumor associated gene product, nucleic acid or polypeptide is one that is identified as expressed in connection with a tumor. As noted by Applicants in the Background of the Invention section of the specification, tumor associated genes are markers for the tumor phenotype. Applicants have demonstrated the tumor associated nature of the gene products, nucleic acids and polypeptides described herein. For example, the Examples provide a description of specific tumor types that the nucleic acids are expressed in. Accordingly, based on the description of tumor associated gene products in the specification and the examples, Applicants maintain that the term "tumor associated" is definite.

The Examiner rejected claims 9, 57 and 58 as indefinite for the use of the phrase "at least a portion." The Examiner has indicated agreement with the use of the commonly accepted definition, but requests that Applicants indicate the location in the specification where "portion" is defined. Applicants respectfully traverse the rejection.

Applicants' are permitted, but not required, to define commonly known words in the specification. The test for determining the definiteness of claim language was set forth in *In re Moore*: "The definiteness of the language must be analyzed -- not in a vacuum, but always in light of the teachings of the prior art and of the particular application as it would be interpreted by on possessing the ordinary level of skill in the pertinent art." *In re Moore* 439 F.2d 1232, 1235 (C.C.P.A. 1971). Many cases have used extrinsic evidence in the form of dictionary definitions of claim terms. Moreover, one of ordinary skill in the art would understand the meaning of "portion" to be consonant with the dictionary definition presented previously by Applicants.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejections made under 35 U.S.C. 112, second paragraph.

Rejections Under 35 U.S.C. 101

The Examiner rejected claims 1, 8, 9, 18, 19, 51-56 and 50 under 35 U.S.C. 101 as lacking utility. The Examiner acknowledged that the utility set forth by Applicants is credible,

but argued that the utility is not specific or substantial. Applicants respectfully disagree, and accordingly traverse the rejection.

The Examiner suggests that one of ordinary skill in the art could not utilize the claimed nucleic acid molecules for diagnosis and/or treatment of conditions because Applicants have not linked the expression of the nucleic acid molecules to any specific tissue. Moreover, the Examiner suggests that Applicants have described the nucleic acid molecules "only indifferently" as tumor associated molecules.

Regarding the Examiner's first point about linking expression of nucleic acids to specific tissues, Applicants respectfully suggest that the Examiner review the Examples provided by Applicants. It may be that the Examiner has misunderstood the teachings of these working examples as they relate to utility. Tables II and III in Example 2 show the expression of sdph3.10 nucleic acids in normal tissues and tumor tissues, respectively. The results depicted in these tables indicated (1) that spdh3.10 is strongly associated with a tumor phenotype (and in fact fit the expression profile of a cancer-testis antigen), and (2) can be used to diagnose at least the tumors in which expression was demonstrated. The results certainly support the use of these nucleic acid molecules in diagnostic assays, and in view of the strongly tumor associated expression pattern, in therapeutic uses as well.

In view of the expression results shown in the Examples, Applicants do not understand the Examiner's suggestion that the nucleic acids and encoded polypeptides could not be used as tumor markers. Tumor associated nucleic acids and polypeptides do not have to be associated with one and only one tumor type as the Examiner appears to be suggesting. Examples of tumor associated nucleic acids and polypeptides that are associated with multiple cancers abound in the literature. Several of the more well-known examples are MAGE-1, MAGE-3, NY-ESO-1, p53 and carcinoembryonic antigen (CEA). These molecules are not only well known, but are highly preferred for diagnostic and therapeutic applications based on their expression in multiple tumors. Expression in multiple tumor types permits the use of these molecules in broad-spectrum assays and therapies. For example, the expression of a molecule such as spdh3.10 in a variety of tumor cells permits one of ordinary skill in the art to design therapies to attack those different kinds of tumor cells, such as monoclonal antibodies (optionally conjugated to cytotoxic agents) and cancer vaccines. Accordingly, the expression patterns demonstrated for the claimed nucleic acid molecules are highly preferred for use by skilled artisans. If the Examiner is in

doubt as to their utility as tumor markers in diagnostic or therapeutic applications, Applicants request an interview to permit the Examiner to ask questions directly of persons skilled in the art as to the utility of the molecules.

In addition to the utility (specific, substantial and credible) of these molecules as tumor markers as set forth above, Applicants did provide other specific, substantial and credible utilities as noted in the response to the previous Office Action. For example, the nucleic acid molecules can be used to synthesize proteins recombinantly. Further, the SAGE (sdph3.10) and sdp3.5 polypeptides can be used alone or as fusion proteins to generate antibodies to SAGE and sdp3.5, and can be used as controls or standards for isolation and/or purification of the SAGE and sdp3.5 from biological extracts (e.g., by chromatography, immunoassay, etc.). The claimed nucleic acid molecules "can be employed to produce nonfused fragments of the tumor associated polypeptides, useful, for example, in the preparation of antibodies, and in immunoassays." Specification at page 14, lines 17-22. The claimed nucleic acids also can be used in PCR amplification (e.g., for expression analysis) as provided in the specification at page 15, line 17 through page 16, line 4. These utilities are specific, substantial and credible, and would be immediately apparent to one of ordinary skill in the art.

As to the Examiner's second point, Applicants wish to point out that the term "tumor associated" is a term of art, which also was described in the Background of the Invention section of the application (page 1). Moreover, the data presented in the Examples showing expression of the sequences in tumor cells, as well as the description in the specification hardly qualifies as "indifferently" describing the claimed nucleic acid molecules as tumor associated.

Based on the same reasons provided above with respect to utility of the claimed invention, Applicants maintain that one of ordinary skill in the art would know how to use the claimed invention in diagnostics, to produce antibodies, to perform PCR analysis, etc.

Accordingly, Applicants respectfully request that the Examiner withdraw the rejection under 35 U.S.C. 101 and 35 U.S.C. 112, first paragraph

Rejections Under 35 U.S.C. 102

The Examiner rejected claims 1, 18, 19, 50 and 59 under 35 U.S.C. 102(b) as anticipated by the nucleotide sequence set forth in GenBank accession number AA213817. The Examiner also rejected claim 60 under 35 U.S.C. 102(b) as anticipated by the nucleotide sequence set forth

in GenBank accession number W86797. Applicants have amended claims 1 and 60 to exclude these sequences. Accordingly, reconsideration and withdrawal of the rejections is respectfully requested.

The Examiner rejected claims 1, 9, 18, 19, 50, and 59 under 35 U.S.C. 102(e) as anticipated by US patent 5,880,102. Applicants respectfully request reconsideration of the rejection for the following reasons.

Nucleotides 975 - 993 and 995 - 1044 of SEQ ID NO:1 of patent 5,880,102 correspond to the extreme 5' end of SEQ ID NO:38 of the instant application. Applicants agree that the '102 patent does not teach explicitly that SEQ ID NO:1 is a vector sequence. In fact, the '102 patent does not describe the origin of SEQ ID NO:1 at all. Accordingly, Applicants performed a search of the nonredundant (nr) database of GenBank to determine the origin of this sequence. The search revealed that the regions of SEQ ID NO: 1 of the '102 patent that matches these short, 5' regions of SEQ ID NO: 38 correspond to numerous vector sequences in the database.
In addition to the evidence indicating that the matching sequence of SEQ ID NO: 1 and the instant SEQ ID NO: 38 are vector sequences, the '102 also patent fails to state any function for the regions containing the sequence matches and also does not teach a nucleic acid molecule that encodes a sarcoma associated antigen (as required by claim 1), or that encodes a portion of SEQ ID NO:39 (as required by claim 9). Accordingly, reconsideration and withdrawal of the rejections is respectfully requested.

Rejections Under 35 U.S.C. 103(a)

The Examiner rejected claims 41 and 57 under 35 U.S.C. 103(a) as unpatentable over US patent 5,880,102. Applicants have amended claim 41 to indicate that the tumor associated polypeptide precursor is one which encodes a portion of SEQ ID NO:39. As described above in the argument related to the anticipation rejection based on the '102 patent, the sequences present in the '102 patent are parts of the vector sequence. These nucleotide sequences do not encode any portion of the polypeptide sequence of sdph3.10 (SAGE), SEQ ID NO:39. Accordingly, Applicants request that the rejection of claims 41 and 57 under 35 U.S.C. 103 be reconsidered and withdrawn.

The Examiner rejected claims 43 and 58 under 35 U.S.C. 103(a) as unpatentable over the nucleotide sequence set forth in GenBank accession number AA213817. Applicants have amended claim 43 to exclude the AA213817 sequence. Claim 58 depends from claim 43. Accordingly, Applicants request that the rejection of claims 43 and 58 under 35 U.S.C. 103 be reconsidered and withdrawn.

Applicants respectfully request reconsideration of the claims in view of the amendments and reasoned statements made above. If the Examiner wishes to advance the prosecution in any way, or if the amendment is defective or unclear, then the Examiner is invited to telephone the undersigned at the telephone number listed below.

Respectfully submitted,

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Docket No. L0461/7047
Dated: March 26, 2001
X03/26/01

Amended Paragraph of the Specification

On page 55:

Alternatively, CTL clones are generated by stimulating the peripheral blood lymphocytes (PBLs) of a patient with autologous normal cells transfected with DNA clones encoding sdph3.10 or sdp3.5 polypeptides (e.g. SEQ ID NOs:38 or 43) or with irradiated PBLs loaded with synthetic peptides corresponding to the putative proteins and matching the consensus for the appropriate HLA class I molecule to localize the antigenic peptide within the sdph3.10 or sdp3.5 clones (see, e.g., van der Bruggen et al., *Eur. J. Immunol.*24:3038-3043, 1994; Herman et al., *Immunogenetics* 43:377-383, 1996). Localization of one or more antigenic peptides in a protein sequence can be aided by HLA peptide binding predictions made according to established rules for binding potential (e.g., Parker et al, *J. Immunol.* 152:163, 1994; Rammensee et al., *Immunogenetics* 41:178-228, 1995). HLA binding predictions can conveniently be made using an algorithm available via the Internet on the National Institutes of Health World Wide Web site [at URL http://bimas.dcrt.nih.gov]. For example, several predicted HLA binding motifs for the sdph3.10 and sdp3.5 polypeptides (SEQ ID NOs:39 and 44) are listed in the table below:

Amended Claims

1. (twice amended) An isolated nucleic acid molecule selected from the group consisting of

(a) nucleic acid molecules which hybridize under stringent conditions to [a nucleic acid molecule having] a nucleotide sequence selected from the group consisting of SEQ ID NO:38 and SEQ ID NO:43, and which code for a sarcoma associated gene product, nucleotides 119-1832 of

(b) nucleic acid molecules that differ from the nucleic acid molecules of [(a)] SEQ ID NO:38 or SEQ ID NO:43 in codon sequence due to the degeneracy of the genetic code, and

(c) complements of (a) and (b),

wherein the isolated nucleic acid molecule excludes nucleic acid molecules consisting of the nucleotide sequence set forth in GenBank accession number AA213817.

40.(amended) A composition comprising:

an antisense nucleic acid which binds to a tumor associated nucleic acid which hybridizes under stringent conditions to a nucleic acid molecule having a nucleotide sequence selected from the group consisting of SEQ ID NO:38 and SEQ ID NO:43, and reduces the expression of the tumor associated nucleic acid[, and

a pharmaceutically acceptable carrier].

41.(twice amended) A kit for detecting the presence of the expression of a tumor associated polypeptide precursor which encodes a portion of SEQ ID NO:39, comprising a first isolated nucleic acid molecule consisting of a 12-32 nucleotide contiguous segment of SEQ ID NO:38, and a second isolated nucleic acid molecule consisting of a 12-32 nucleotide contiguous segment of the complement of SEQ ID NO:38, wherein the contiguous segments are nonoverlapping.

43.(thrice amended) A kit for detecting the presence of the expression of a tumor associated polypeptide precursor encoded by SEQ ID NO:43, comprising a first isolated nucleic acid molecule consisting of a 12-32 nucleotide contiguous segment of SEQ ID NO:43, and a second isolated nucleic acid molecule consisting of a 12-32 nucleotide contiguous segment of the complement of SEQ ID NO:43, wherein the contiguous segments are nonoverlapping, and wherein the first and second isolated nucleic acid molecules exclude nucleic acid molecules consisting of segments of the nucleotide sequence set forth in GenBank accession number AA213817.

60. (amended) An isolated nucleic acid molecule selected from the group consisting of

(a) nucleic acid molecules which hybridize under stringent conditions to a nucleic acid molecule having a nucleotide sequence set forth as SEQ ID NO:1, and which code for a sarcoma associated gene product,

(b) nucleic acid molecules that differ from the nucleic acid molecules of (a) in codon sequence due to the degeneracy of the genetic code, and

(c) complements of (a) and (b),

wherein the isolated nucleic acid molecule excludes nucleic acid molecules completely composed of the nucleotide sequence of GenBank accession number W86797.